

Amendments to the Specification

Please replace the paragraph at page 11, lines 29 through 31 with the following amended paragraph:

Figure 53 shows the amino acid sequence (SEQ ID NO:2) of the heavy chain V region and the amino acid sequence (SEQ ID NO:4) of the light (kappa) chain V region of human monoclonal antibody 2F2 with CDR regions (SEQ ID NOs:13-18) designated.

Please replace the paragraph at page 11, lines 35 through 37 with the following amended paragraph:

Figure 55 shows the amino acid sequence (SEQ ID NO:6) of the heavy chain V region and the amino acid sequence (SEQ ID NO:8) of the light (kappa) chain V region of human monoclonal antibody 7D8 with CDR regions (SEQ ID NOs:19-24) designated.

Please replace the paragraph at page 12, lines 4 through 6 with the following amended paragraph:

Figure 57 shows the amino acid sequence (SEQ ID NO:10) of the heavy chain V region and the amino acid sequence (SEQ ID NO:12) of the light (kappa) chain V region of human monoclonal antibody 11B8 with CDR regions (SEQ ID NOs:25-30) designated.

Please replace the paragraph at page 13, lines 12 through 20 with the following amended paragraph:

In yet another embodiment the invention relates to human polyclonal antibodies which bind to an epitope in the small first extracellular loop of human CD20. In still another embodiment the invention also encompasses human polyclonal antibodies which bind to a discontinuous epitope on CD20. In a further embodiment the invention relates to human polyclonal antibodies which bind a discontinuous epitope on CD20, which has part of the first small extracellular loop and part of the second extracellular loop. In still a further embodiment the invention relates to human polyclonal antibodies which bind to a discontinuous epitope on CD20, which has residues AGIYAP (SEQ ID NO:93) of the small first extracellular loop and residues MESLNFIRAHTPYI (SEQ ID NO:94) of the second extracellular loop.

Please replace the paragraph at page 63, lines 18 through 26 with the following amended paragraph:

cDNA preparation of 2F2 and 7D8: 5'-RACE-Ready Complementary DNA (cDNA) of RNA was prepared from 1 µg total RNA, using the SMART RACE cDNA Amplification kit (Clontech), following the manufacturer's protocol.

V_H and V_L regions were amplified using an advantage HF 2 PCR Kit (Clontech, BD) and using the following primers:

V_K RACE2 5' GCA GGC ACA CAA CAG AGG CAG TTC CAG ATT TC (SEQ ID NO:31) anneals in C-kappa
V_H RACE2 5' GCT GTG CCC CCA GAG GTG CTC TTG GAG G (SEQ ID NO:32) anneals in C_{H1}

Please replace the paragraph at page 64, lines 1 through 37 with the following amended paragraph:

PCR primers used to amplify V_H and V_L regions for cloning:

Primer pairs used:

V_H: FR1 5' primers

AB62 CAg gTK CAg CTg gTg CAg TC (SEQ ID NO:33)

AB63 SAg gTg CAg CTg KTg gAg TC (SEQ ID NO:34)

AB65 gAg gTg CAg CTg gTg CAg TC (SEQ ID NO:35)

V_H leader 5' primers

AB85 ATg gAC Tgg ACC Tgg AgC ATC (SEQ ID NO:36)

AB86 ATg gAA TTg ggg CTg AgC Tg (SEQ ID NO:37)

AB87 ATg gAg TTT ggR CTg AgC Tg (SEQ ID NO:38)

AB88 ATg AAA CAC CTg Tgg TTC TTC (SEQ ID NO:39)

AB89 ATg ggg TCA ACC gCC ATC CT (SEQ ID NO:40)

V_H 3' primer

AB90 TgC CAg ggg gAA gAC CgA Tgg (SEQ ID NO:41)

V_K:FR1 5' primers

AB8 RAC ATC CAg ATg AYC CAg TC (SEQ ID NO:42)
AB9 gYC ATC YRg ATg ACC CAg TC (SEQ ID NO:43)
AB10 gAT ATT gTg ATg ACC CAg AC (SEQ ID NO:44)
AB11 gAA ATT gTg TTg ACR CAg TC (SEQ ID NO:45)
AB12 gAA ATW gTR ATg ACA CAg TC (SEQ ID NO:46)
AB13 gAT gTT gTg ATg ACA CAG TC (SEQ ID NO:47)
AB14 gAA ATT gTg CTg ACT CAg TC (SEQ ID NO:48)

V_K leader 5' primers

AB123 CCC gCT Cag CTC CTg ggg CTC CTg (SEQ ID NO:49)
AB124 CCC TgC TCA gCT CCT ggg gCT gC (SEQ ID NO:50)
AB125 CCC AgC gCA gCT TCT CTT CCT CCT gC (SEQ ID NO:51)
AB126 ATg gAA CCA Tgg AAg CCC CAg CAC AgC (SEQ ID NO:52)

V_K 3' primer

AB16 Cgg gAA gAT gAA gAC AgA Tg (SEQ ID NO:53)

wherein K = T or G, S = C or G, R = A or G, Y = C or T, and W = A or T.

Please replace the Table 3 at page 91, lines 21 through 24 with the following amended Table 3:

Table 3

Name	Application	Length	Oligo Sequence	<u>SEQ ID NOs</u>
CD20P172S	CD20 mutagenesis	36	TGGGGAGTTTTTCTCAGAGGAATTCGATGGTTCACAGTT GTA	<u>SEQ ID NO:58</u>
CD20N166D	CD20 mutagenesis	39	TGTAACAGTATTGGGTAGATGGG	<u>SEQ ID NO:59</u>
CD20N163D	CD20 mutagenesis	36	AATCATGGACATACTTAATATTA	<u>SEQ ID NO:60</u>
cd20exfor	CD20 construction	41	TATAGCCCGGGGCCGCCACCATGACAACACCCAGAAAT TCA	<u>SEQ ID NO:61</u>
cd20exrev	CD20 construction	38	GCGTCTCATGTACATTAAGGAGAGCTGTCATTTTCTAT	<u>SEQ ID NO:62</u>
pee13.4seqrev2	Colony PCR	23	TCGGACATCTCATGACTTTCTTT	<u>SEQ ID NO:63</u>
pConKseq1	Colony PCR	23	GTAGTCTGAGCAGTACTCGTTGC	<u>SEQ ID NO:64</u>
cd20hsapmutr (AxP)	CD20 mutagenesis	42	TGGGGAGTTTTTCTCAGAGGAATTCGATGGTTCACAGTT GTA	<u>SEQ ID NO:65</u>
cd20hsapmutf (AxP)	CD20 mutagenesis	42	TACAACTGTGAACCATCGAATTCCTCTGAGAAAAACTC CCCA	<u>SEQ ID NO:66</u>
CD20seq2	CD20 sequencing	23	TGTAACAGTATTGGGTAGATGGG	<u>SEQ ID NO:67</u>
cd20seq1	CD20 sequencing	23	AATCATGGACATACTTAATATTA	<u>SEQ ID NO:68</u>

Please replace Table 4 and 5 at page 94, line 13 through page 96, line 4 with the following amended Table 4 and 5:

Table 4

		mABs									
Amino Acid Sequence	SEQ ID NOs	11B8 10 µg/ml	11B8 100 µg/ml	7D8 10 µg/ml	7D8 100 µg/ml	7D8 10 µg/ml	rituximab 10 µg/ml	2F2 10 µg/ml	2F2 100 µg/ml	B1 10 µg/ml	B1 100 µg/ml
KMECLNFIRAHCPYI	SEQ ID NO:69	763	2997	134	41	90	48	66	147	304	
LKMECLNFIRCHTPY	SEQ ID NO:70	165	738	160	41	120	49	87	179	216	
KMESCNFIRACTPYI	SEQ ID NO:71	625	3090	142	52	123	39	78	170	308	
MESLCFIRAHCPYIN	SEQ ID NO:72	179	956	127	55	102	41	65	119	178	
CFIRAHTPC	SEQ ID NO:73	188	534	181	69	134	91	114	170	212	
CIRAHTPYC	SEQ ID NO:74	151	449	186	60	132	57	92	151	195	
CRAHTPYIC	SEQ ID NO:75	427	1605	188	64	145	48	87	179	216	
CAHTPYINC	SEQ ID NO:76	179	452	174	65	125	42	106	161	172	
IPAGIYA	SEQ ID NO:77	217	950	164	76	177	48	85	165	192	
PAGIYAP	SEQ ID NO:78	449	2501	170	64	111	43	85	165	300	
AGIYAPI	SEQ ID NO:79	251	2207	188	73	110	44	98	187	143	
GIYAPIC	SEQ ID NO:80	99	251	152	64	141	34	93	177	147	
IYAPICV	SEQ ID NO:81	137	313	174	58	159	58	99	175	90	
GIYAPIA	SEQ ID NO:82	172	857	177	96	156	62	96	165	121	
IYAPIAV	SEQ ID NO:83	161	654	181	58	116	62	76	161	106	

Table 5

Amino Acid Sequence	SEQ ID NOs	mABs			
		11B8 10 µg/ml	7D8 10 µg/ml	rituximab 10 µg/ml	2F2 10 µg/ml
PCINIYNAEPANPCE	<u>SEQ ID NO:84</u>	118	163	152	65
YCNIYNAEPANPSCK	<u>SEQ ID NO:85</u>	287	181	2418	86
ICIYNAEPANPSECN	<u>SEQ ID NO:86</u>	138	192	142	78
NCYNAEPANPSEKCS	<u>SEQ ID NO:87</u>	93	121	2649	49
ICNAEPANPSEKNCP	<u>SEQ ID NO:88</u>	115	165	3283	43
YCAEPANPSEKNSCS	<u>SEQ ID NO:89</u>	106	188	3770	65
NCEPANPSEKNSPCT	<u>SEQ ID NO:90</u>	159	183	3476	61
ACPANPSEKNSPSCQ	<u>SEQ ID NO:91</u>	146	148	250	77
ECANPSEKNSPSTCY	<u>SEQ ID NO:92</u>	134	179	188	68

Please replace the paragraph at page 96, lines 5 through 7 with the following amended paragraph:

As appears from Table 4, 11B8 showed binding to AGIYAP (SEQ ID NO:93) of the small first extracellular loop of human CD20 at both 10 µg/ml and 100 µg/ml, whereas the other antibodies tested did not show significant binding to AGIYAP (SEQ ID NO:93).

Please replace the paragraph at page 96, lines 8 through 10 with the following amended paragraph:

Furthermore, 11B8 showed binding to MESLNFIRAHTPYI (SEQ ID NO:94) of the second extracellular loop of human CD20 at both 10 µg/ml and 100 µg/ml, whereas the other antibodies tested did not show significant binding to MESLNFIRAHTPYI (SEQ ID NO:94).

Please replace the paragraph at page 96, lines 11 through 13 with the following amended paragraph:

As appears from Table 5, rituximab showed binding to EPANPSEK (SEQ ID NO:95) of the second extracellular loop of human CD20 at both 1 µg/ml and 10 µg/ml, whereas the other antibodies tested did not show significant binding to EPANPSEK (SEQ ID NO:95).